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PATENTS

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:

Alan Patterson et al.

Serial No.: ~~08/765,475~~ 09/159,680

Filed: ~~January 9, 1997~~ September 24, 1998

For: LONG-ACTING OXYTETRACYCLINE COMPOSITION

Group Art Unit: 1614

Examiner: J. Goldberg



**RESPONSE**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the Office Action mailed on October 27, 1998.

With respect to the provisional double patenting rejection, the applicants point out that the copending Application No. 08/765,475 is now abandoned.

Reconsideration of the rejection of claims 1-9 and 11-21 under 35 U.S.C. 103 as being unpatentable over Zupan et al. in view of EP 0038013 and Malook et al. is respectfully requested. All of the claims call for a composition having a water miscible solvent system comprising glycerol formal and polyethylene glycol in specific amounts. The combination of references set forth by the Examiner requires the use of a certain percentage of polyethylene glycol in the range disclosed by Zupan et al. with a certain percentage of glycerol formal in the



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range disclosed in the European reference. However, the applicants submit that it would not have been obvious merely to choose an amount of polyethylene glycol disclosed in one reference and combine it with an amount of glycerol formal disclosed in another reference for the reason that the effect of such choosing and combining is unpredictable. In support of this position, the applicants' submit herewith the declaration of Dr. Sean Duffy. As can be seen from the bottom half of the second page of his declaration and from the third page, Dr. Duffy made two formulations containing an amount of polyethylene glycol 400 from the range disclosed in Zupan et al. and made it to volume with glycerol formal from the European reference. As Dr. Duffy states beginning at the bottom of the fourth page of his declaration, both formulations were dark in color and exhibited great difficulty in filtration. In addition, the syringeability of both formulations was completely unsatisfactory using the conventional test of syringeability. In the third statement on the fourth page, Dr. Duffy states that, due to these physical characteristics, neither formulation would be a viable commercial product and would not have been taken as far as the stage in which animal field trials are conducted.

The fourth and fifth pages of the declaration compare formulations 1 and 2 described above, after they were stored at room temperature for five months, with two samples of the composition of the present invention, one of which was manufactured in 1996 and the other of which was freshly prepared. Sediment formed in formulations 1 and 2, but not in the samples of the present invention. Formulations 1 ane 2 failed the syringeability test which the samples of the present invention passed.

It is submitted that the declaration shows that one having ordinary skill in the art cannot merely choose any amount of polyethylene glycol in the range disclosed in Zupan et al. and just

any amount of glycerol formal from the range disclosed in the European reference and have a commercially viable product, much less a product which has improved performance over previously known commercial products.

On pages 6-8 of the declaration, pharmacokinetic study data in cattle for Product No. 040, a composition according to the present invention, and two other formulations considered to have commercial potential are shown. It can be seen from the data that the maximum concentration of oxytetracycline in bovine plasma is improved with Product No. 040, the composition according to the present invention. It can also be seen from pharmacokinetic study data for pigs on pages 8 and 9 of the declaration that the product according to the present invention, Product No. AL-040, had a higher maximum concentration in porcine plasma and greater overall distribution over time than a composition containing 30% glycerol formal and 20% polyethylene glycol 200. 20% polyethylene glycol 200 is 5% higher than the range of polyethylene glycol called for in the claims of the present application.

On page 9, Dr. Duffy states that compositions according to the present invention having a water miscible solvent system comprising glycerol formal in an amount from about 10 to about 50% v/v and polyethylene glycol in an amount from about 1 to 15% v/v provided effective levels of tetracycline compound in bovine plasma for more than 9 days. For purposes of comparison, Dr. Duffy states that previously known products have provided levels of the tetracycline compound in plasma for only up to about four days. Furthermore, he indicates on the same page that, based on his level of skill, he would not expect the interchanging of solvents in general or the addition of polyethylene glycol in an amount disclosed in Zupan et al. to glycerol formal in an amount disclosed in the European reference to have any foreseeable benefit.

In view of the foregoing, it is submitted that it would not have been obvious to add just any amount of the polyethylene glycol from the range disclosed in Zupan et al. to glycerol formal in any amount from the range disclosed in the European reference. It is submitted that the declaration of Dr. Duffy indicates that at least some chosen amounts from these ranges do not produce a commercially viable product. Furthermore, there is no suggestion in the prior art as to which amounts of the solvents from the ranges disclosed in these references would provide a commercially viable product when added together. Accordingly, it is submitted that the compositions of the present claims are unobvious and patentable.

A Notice of Allowance is respectfully requested.

Respectfully submitted,

Date: 3-16-99

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231, on the date of signature identified below.

John P. Shannon, Reg. No. 29,276

Signature

Date of Signature 3-16-99